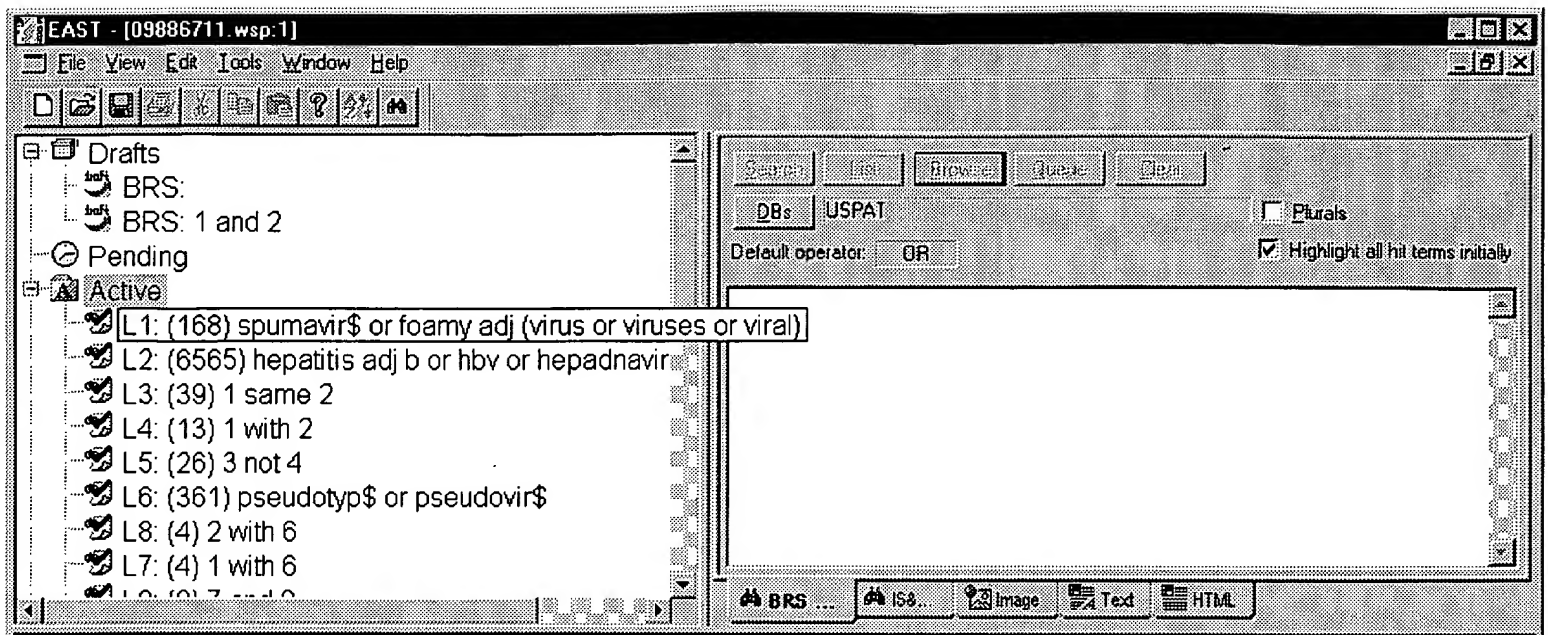

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1	BRS	L1	168	spumavir$ or foamy adj (virus or viruses or viral)	USPAT	2002/04/30 11:50
2	BRS	L2	6565	hepatitis adj b or hbv or hepadnavir$	USPAT	2002/04/30 11:50
3	BRS	L3	39	1 same 2	USPAT	2002/04/30 11:39
4	BRS	L4	13	1 with 2	USPAT	2002/04/30 11:40
5	BRS	L5	26	3 not 4	USPAT	2002/04/30 11:42
6	BRS	L6	361	pseudotyp$ or pseudovir$	USPAT	2002/04/30 11:53
7	BRS	L8	4	2 with 6	USPAT	2002/04/30 11:47
8	BRS	L7	4	1 with 6	USPAT	2002/04/30 11:47
9	BRS	L9	0	7 and 8	USPAT	2002/04/30 11:47
10	BRS	L10	5	2 same 6	USPAT	2002/04/30 11:48
11	BRS	L11	7	1 same 6	USPAT	2002/04/30 11:47
12	BRS	L12	1	10 not 8	USPAT	2002/04/30 11:48
13	BRS	L14	3	11 not 7	USPAT	2002/04/30 11:49
14	BRS	L15	52	spumavir$ or foamy adj (virus or viruses or viral)	US-PGPUB; EPO; JPO; DERWENT	2002/04/30 11:50
15	BRS	L16	4113	hepatitis adj b or hbv or hepadnavir$	US-PGPUB; EPO; JPO; DERWENT	2002/04/30 11:50
16	BRS	L17	7	15 and 16	US-PGPUB; EPO; JPO; DERWENT	2002/04/30 11:50
17	BRS	L18	156	pseudotyp$ or pseudovir$	US-PGPUB; EPO; JPO; DERWENT	2002/04/30 11:53
18	BRS	L19	9	18 same (15 or 16)	US-PGPUB; EPO; JPO; DERWENT	2002/04/30 11:53
19	BRS	FAMILY	1	2001-201505.NRAN.	DERWENT	2002/04/30 11:57

? b 155,357
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$0.28 0.081 DialUnits File1
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$0.29 Estimated cost this search
$0.29 Estimated total session cost 0.081 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-2002/Apr W3
*File 155: This file will be reloaded. Accession numbers will change.
File 357:Derwent Biotech Res 1982-2002/Feb w3
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*File 357: Price changes as of 1/1/02. Please see HELP RATES 357.
Derwent announces file enhancements. Please see HELP NEWS 357.

Set Items Description
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? ds
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S1 43936 HEPATITIS(W)B OR HBV OR HEPADNAVIR?
S2 1467 FOAMY
S3 11 S1 AND S2
S4 433 SPUMA?
S5 12 S1 AND S4
S6 2 S5 NOT S3
S7 34707 CHIMER? OR CHIMAER? OR PSEUDOVIR?
S8 22 S7 AND (S2 OR S4)
S9 1035 PSEUDOTYP?
S10 12 S9 AND (S2 OR S4) NOT S8
S11 10 RD (unique items)
S12 7 PSEUDO AND (S2 OR S4)
S13 4 PSEUDO? AND RETROVIR? AND S1
S14 1178 PSEUDOTYP? OR PSEUDOVIR?
S15 12 14 AND RETROVIR? AND S1
S16 10 S14 AND RETROVIR? AND S1
? t s3/7/1-11
3/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
11576244 21329467 PMID: 11435565
Identification of a conserved residue of foamy virus Gag required for intracellular capsid assembly.
Eastman SW; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109, USA.
Journal of virology (United States) Aug 2001, 75 (15) p6857-64, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA18282, CA, NCI; T32 0229, PHS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In contrast to all retroviruses but similar to the hepatitis B virus, foamy viruses (FV) require expression of the envelope protein for budding of intracellular capsids from the cell, suggesting a specific interaction between the Gag and Env proteins. Capsid assembly occurs in the cytoplasm of infected cells in a manner similar to that for the B- and D-type viruses; however, in contrast to these retroviruses, FV Gag lacks an N-terminal `myristylation signal and capsids are not targeted to the plasma membrane (PM). We have found that mutation of an absolutely conserved arginine (Arg) residue at position 50 to alanine (R50A) of the simian foamy virus SFV cpz(hu) inhibits proper capsid assembly and abolishes viral budding even in the presence of the envelope (Env) glycoproteins. Particle assembly and extracellular release of virus can be restored to this mutant with the addition of an N-terminal Src myristylation signal (Myr-R50A), presumably by providing an alternate site for assembly to occur at the PM. In addition, the strict requirement of Env expression for capsid budding can be bypassed by addition of a PM-targeting signal to Gag. These results suggest that intracellular capsid assembly may be mediated by a signal akin to the cytoplasmic targeting and retention signal CTRS found in Mason-Pfizer monkey virus and that FV Gag has the inherent ability to assemble capsids at multiple sites like conventional retroviruses. The necessity of Env expression for particle egress is most probably due to the lack of a membrane-targeting signal within FV Gag to direct capsids to the PM for release and indicates that Gag-Env interactions are essential to drive particle budding.
Record Date Created: 20010703

3/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10494489 20111290 PMID: 10644342
Multiple integrations of human foamy virus in persistently infected human erythroleukemia cells.
Meiering CD; Comstock KE; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109, USA.
Journal of virology (UNITED STATES) Feb 2000, 74 (4) p1718-26, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: P01 HL53762, HL, NHLBI; R01 CA18282, CA, NCI; T32 GM07270, GM, NIGMS; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Foamy viruses are complex retroviruses whose replication strategy resembles that of conventional retroviruses. However, foamy virus

replication also resembles that of hepadnaviruses in many respects. Because hepadnaviruses replicate in an integrase-independent manner, we were interested in investigating the characteristics of human foamy virus (HFV) integration. We have shown that HFV requires a functional integrase protein for infectivity. Our analyses have revealed that in single-cell clones derived from HFV-infected erythroleukemia-derived cells (H92), there were up to 20 proviral copies per host cell genome as determined by Southern blot and fluorescent in situ hybridization analysis. Use of specific probes has also shown that a majority of the proviruses contain the complete tas gene, which encodes the viral transactivator, and are not derived from Deltatas cDNAs, which have been shown to arise rapidly in infected cells. To demonstrate that the multiple proviral sequences are due to integration instead of recombination, we have sequenced the junctions between the proviral sequences and the host genome and found that the proviruses have authentic long terminal repeat ends and that each integration is at a different chromosomal site. A virus lacking the Gag nuclear localization signal accumulates fewer proviruses, suggesting that nuclear translocation is important for high proviral load. Since persistently infected H92 clones are not resistant to superinfection, the relative importance of an intracellular versus extracellular mechanism in proviral acquisition has yet to be determined.
Record Date Created: 20000302

3/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10225419 99329158 PMID: 10400731
Proteolytic activity, the carboxy terminus of Gag, and the primer binding site are not required for Pol incorporation into foamy virus particles.
Baldwin DN; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109, USA.
Journal of virology (UNITED STATES) Aug 1999, 73 (8) p6387-93, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA18282, CA, NCI; T32 GM07270, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human foamy virus (HFV) is the prototype member of the spumaviruses. While similar in genomic organization to other complex retroviruses, foamy viruses share several features with their more distant relatives, the hepadnaviruses such as human hepatitis B virus (HBV). Both HFV and HBV express their Pol proteins independently from the structural proteins. However unlike HBV, Pol is not required for assembly of HFV core particles or for packaging of viral RNA. These results suggest that the assembly of Pol into HFV particles must occur by a mechanism different from those used by retroviruses and hepadnaviruses. We have examined possible mechanisms for HFV Pol incorporation, including the role of proteolysis in assembly of Pol and the role of initiation of reverse transcription. We have found that proteolytic activity is not required for Pol incorporation. p4 Gag and the residues immediately upstream of the cleavage site in Gag are also not important. Deletion of the primer binding site had no effect on assembly, ruling out early steps of reverse transcription in the process of Pol incorporation.
Record Date Created: 19990824

3/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10166801 99301498 PMID: 10374962
An active foamy virus integrase is required for virus replication.
Enssle J; Moebes A; Heinkelein M; Panhuysen M; Mauer B; Schweizer M; Neumann-Haefelin D; Rethwilm A
Institut fur Virologie und Immunbiologie, Universitat Wurzburg, Germany.
Journal of general virology (ENGLAND) Jun 1999, 80 (Pt 6) p1445-52, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Foamy viruses (FVs) make use of a replication strategy which is unique among retroviruses and shows analogies to hepadnaviruses. The presence of an integrase (IN) and obligate provirus integration distinguish retroviruses from hepadnaviruses. To clarify whether a functional IN is required for FV replication, a mutant in the highly conserved DD35E motif of the active centre was analysed. This mutant was found to be able to express Gag and Pol protein precursors and cleavage products and to generate and deliver cDNA. However, this mutant was replication-deficient. The junctions of individual foamy proviruses with cellular DNA were sequenced. The findings suggest that FV integration is asymmetrical, because the proviruses started with what is believed to be the U3 end of the free linear DNA to generate the conventional TG dinucleotide, while apparently two nucleotides from the U5 end were cleaved to create the complementary CA dinucleotide. Alignment of known FV genome sequences indicated that this mechanism of integration is not restricted to the two FV isolates from which integrates were studied, but appears to be a common feature of this retrovirus subfamily. In conclusion, with respect to the necessity of a functionally active IN for virus replication FVs behave like other retroviruses; their mechanism of integration, however, is probably unique.
Record Date Created: 19990629

3/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10019930 99099048 PMID: 9882362
Evidence that the human foamy virus genome is DNA.
Yu SF; Sullivan MD; Linial ML

Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109, USA.
Journal of virology (UNITED STATES) Feb 1999, 73 (2) p1565-72, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA 18282, CA, NCI; HL 53753, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The genomes of the spumaviruses, of which human foamy virus (HFV) is the prototype, are very similar to those of other complex retroviruses. However, in some aspects of the viral replicative cycle, HFV more closely resembles pararetroviruses such as hepatitis B virus. Previous work indicated that HFV extracellular particles contain apparently full-length double-stranded DNA, as well as RNA. We have further characterized the amount of DNA in particles and the role that this DNA has in viral replication. Experiments with the reverse transcriptase inhibitor 3'-azido-3'-deoxythymidine (AZT) suggest that reverse transcription is largely complete before extracellular virus infects new cells. In addition, we have been able to show that DNA extracted from virions can lead to production of virus after transfection. Taken together, these data suggest that complete, or nearly complete, proviral-length DNA is present in viral particles and that this DNA is sufficient for new rounds of viral replication.
Record Date Created: 19990218

3/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09735549 98216724 PMID: 9557646
The roles of Pol and Env in the assembly pathway of human foamy virus.
Baldwin DN; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98104, USA.
Journal of virology (UNITED STATES) May 1998, 72 (5) p3658-65, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA18282, CA, NCI; T32 GM07270, GM, NIGMS
Comment in J Virol. 1999 Oct;73(10) 8917
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human foamy virus (HFV) is the prototype of the Spumavirus genus of retroviruses. These viruses have a genomic organization close to that of other complex retroviruses but have similarities to hepadnaviruses such as human hepatitis B virus (HBV). Both HFV and HBV express their Pol protein independently of their structural proteins. Retroviruses and hepadnaviruses differ in their requirements for particle assembly and genome packaging. Assembly of retroviral particles containing RNA genomes requires only the Gag structural protein. The Pol protein is not required for capsid assembly, and the Env surface glycoprotein is not required for release of virions from the cell. In contrast, assembly of extracellular HBV particles containing DNA requires core structural protein and polymerase (P protein) for assembly of nucleocapsids and requires surface glycoproteins for release from the cell. We investigated the requirements for synthesis of extracellular HFV particles by constructing mutants with either the pol or env gene deleted. We found that the Pol protein is dispensable for production of extracellular particles containing viral nucleic acid. In the absence of Env, intracellular particles are synthesized but few or no extracellular particles could be detected. Thus, foamy virus assembly is distinct from that of other reverse transcriptase-encoding mammalian viruses.
Record Date Created: 19980520

3/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09591846 97456493 PMID: 9311807
Human foamy virus reverse transcription that occurs late in the viral replication cycle.
Moebes A; Enssle J; Bieniasz PD; Heinkelein M; Lindemann D; Bock M; McClure MO; Rethwilm A
Institut fur Virologie und Immunbiologie, Universitat Wurzburg, Germany.
Journal of virology (UNITED STATES) Oct 1997, 71 (10) p7305-11, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Foamy viruses (FVs) are retroid viruses which use a replication strategy unlike those of other retroviruses and hepadnaviruses (S. F. Yu, D. N. Baldwin, S. R. Gwynn, S. Yendapilli, and M. L. Linial, Science 271:1579-1582, 1996). One of the striking differences between FVs and retroviruses is the presence of large amounts of linear genome-length DNA in FV-infected cells and in virions. We report here that large quantities of genome-length linear FV DNA accumulate in cells infected with FV, as determined by Southern blotting. To determine whether these unintegrated virus DNAs result solely from superinfection, we analyzed the occurrence of virus cDNA of the so-called human FV isolate (HFV) in cells transfected with a virus mutant deficient in the envelope gene and in cells which are resistant to superinfection due to stable expression of the envelope protein. We show that the synthesis of viral cDNA is independent of superinfection and that HFV synthesizes cDNA intracellularly as a late event in the replication cycle. To further confirm this finding, we performed inhibition studies with the reverse transcriptase inhibitor zidovudine (AZT). While AZT had no effect or only a minor effect on virus titers when added to cells prior to virus infection, viral titers were reduced by 3 or 4 orders of magnitude when the virus was produced from cells in the presence of AZT. Our results are most compatible with the

hypothesis that the functional nucleic acid of the extracellular HFV consists of largely double-stranded linear DNA.
Record Date Created: 19971020

3/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09198196 97126020 PMID: 8970944
The carboxyl terminus of the human foamy virus Gag protein contains separable nucleic acid binding and nuclear transport domains.
Yu SF; Edelmann K; Strong RK; Moebes A; Rethwilm A; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98104, USA.
Journal of virology (UNITED STATES) Dec 1996, 70 (12) p8255-62, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA18282, CA, NCI; F32 CA60357, CA, NCI; HL53763, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The Gag protein of human foamy virus (HFV) lacks Cys-His boxes present in the nucleocapsid (NC) domains of other retroviruses; instead it contains three glycine-arginine-rich motifs (GR boxes). We have expressed the carboxyl end of HFV Gag containing the GR boxes (the NC domain equivalent) and analyzed its nucleic acid binding properties. Our results show that the NC domain of HFV Gag binds with high affinity to both RNA and DNA, in a sequence-independent manner, as determined by filter binding assays. Analysis of a mutant containing a heterologous sequence in place of GR box I indicates that this motif is required for nucleic acid binding and for viral replication. A mutant in GR box II still binds to RNA and DNA in vitro, but virus containing this mutation does not replicate and no nuclear staining of the Gag protein is found in transfected cells. Surprisingly, a revertant from this mutant that completely lacks GR box II and exhibits very little nuclear transport of Gag can readily replicate in tissue culture. This finding thus provides a direct evidence that although the sequences in GR box II can serve as a nuclear transport signal, they are not required for HFV replication and it is unlikely that nuclear localization of Gag protein plays any critical role during viral infection. Taken together, our results suggest that the Gag protein of HFV may be more analogous to the core protein of the hepatitis B virus family than to conventional retroviral Gag protein.
Record Date Created: 19970123

3/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09000858 96390758 PMID: 8797731
Unexpected replication pathways of foamy viruses.
Rethwilm A
Institut fur Virologie und Immunbiologie, Wurzburg, Germany.
Journal of acquired immune deficiency syndromes and human retrovirology (UNITED STATES) 1996, 13 Suppl 1 pS248-53, ISSN 1077-9450
Journal Code: B7J
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Foamy viruses make up a distinct subgroup of retroviruses. They are widely distributed among nonhuman primates, felines, and bovines. In their natural hosts and in cases of rare zoonotic transmissions to humans foamy viruses cause persistent and apparently benign infections. While foamy viruses are not of medical importance in causing human or animal diseases, they may become valuable tools for somatic gene transfer in the future. However, a better understanding of the molecular biology of this virus group is a prerequisite for the development of foamy virus vectors. In this respect, recent research has revealed major differences between the foamy virus and the general retroviral replication strategies and some similarities to hepadnaviruses. (52 Refs.)
Record Date Created: 19961029

3/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
08882099 96179446 PMID: 8599113
Human foamy virus replication: a pathway distinct from that of retroviruses and hepadnaviruses.
Yu SF; Baldwin DN; Gwynn SR; Yendapalli S; Linial ML
Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA 98104, USA.
Science (UNITED STATES) Mar 15 1996, 271 (5255) p1579-82, ISSN 0036-8075 Journal Code: UJ7
Contract/Grant No.: CA18282, CA, NCI; F32 CA60357, CA, NCI; HL53762, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human foamy virus (HFV) is the prototype of the Spumavirus genus of Retroviridae. In all other retroviruses, the pol gene products, including reverse transcriptase, are synthesized as Gag-Pol fusion proteins and are cleaved to functional enzymes during viral budding or release. In contrast, the Pol protein of HFV is translated from a spliced messenger RNA and lacks Gag domains. Infectious HFV particles contain double-stranded DNA similar in size to full-length provirus, suggesting that reverse transcription has taken place in viral particles before new rounds of infection, reminiscent of hepadnaviruses. These data suggest that foamy viruses possess a replication pathway containing features of both retroviruses and hepadnaviruses but distinct from both.
Record Date Created: 19960425

3/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
05877922 86127625 PMID: 3511726
Pathologic and ultrastructural changes of acute and chronic delta hepatitis in an experimentally infected chimpanzee.
Govindarajan S; Fields HA; Humphrey CD; Margolis HS
American journal of pathology (UNITED STATES) Feb 1986, 122 (2) p315-22, ISSN 0002-9440 Journal Code: 3RS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A hepatitis B surface antigen (HBsAg) chronic carrier chimpanzee experimentally superinfected with delta virus (DV) developed chronic DV infection. Over a period of 12 months, serologic and biochemical changes were correlated with morphologic abnormalities of the liver. Severe hepatic necrosis and inflammation accompanied the initial acute episode of hepatitis on Day 35 after inoculation, followed by complete resolution of these lesions over the next 3 months. A second episode of hepatitis occurred on Day 145, and severe necrosis and inflammation recurred along with the reappearance of delta antigen in the hepatocytes. Delta antigen persisted in the liver following the second episode of hepatitis and has remained positive throughout the observation period of 1 year. During the initial acute episode, the hepatocytes exhibited foamy cytoplasmic changes resembling microvesicular fat. However, ultrastructural studies of the same cells revealed only vacuolization of the cytoplasm without evidence of fat droplets. The inflammatory infiltrate during both episodes of hepatitis demonstrated a striking predominance of macrophages over lymphocytes. Hepatocyte abnormalities observed by electron microscopy included vacuoles, proliferated endoplasmic reticulum, and tubules similar to those seen in posttransfusion non-A, non-B hepatitis. However, the tubular and reticular abnormalities coincided with delta antigen expression in liver biopsies detected by direct immunoperoxidase staining and abnormal alanine aminotransferase levels in the serum, which suggests a possible causal relationship. Nuclear abnormalities were not seen.
Record Date Created: 19860317
? t s6/7/1 2
6/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
05843127 88188241 PMID: 2451755
Analysis of the primary structure of the long terminal repeat and the gag and pol genes of the human spumaretrovirus.
Maurer B; Bannert H; Darai G; Flugel RM
Institut fur Virusforschung, Deutsches Krebsforschungszentrum, Heidelberg, Federal Republic of Germany.
Journal of virology (UNITED STATES) May 1988, 62 (5) p1590-7, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The nucleotide sequence of the human spumaretrovirus (HSRV) genome was determined. The 5' long terminal repeat region was analyzed by strong stop cDNA synthesis and S1 nuclease mapping. The length of the RU5 region was determined and found to be 346 nucleotides long. The 5' long terminal repeat is 1,123 base pairs long and is bound by an 18-base-pair primer-binding site complementary to the 3' end of mammalian lysine-1,2-specific tRNA. Open reading frames for gag and pol genes were identified. Surprisingly, the HSRV gag protein does not contain the cysteine motif of the nucleic acid-binding proteins found in and typical of all other retroviral gag proteins; instead the HSRV gag gene encodes a strongly basic protein reminiscent of those of hepatitis B virus and retrotransposons. The carboxy-terminal part of the HSRV gag gene products encodes a protease domain. The pol gene overlaps the gag gene and is postulated to be synthesized as a gag/pol precursor via translational frameshifting analogous to that of Rous sarcoma virus, with 7 nucleotides immediately upstream of the termination codons of gag conserved between the two viral genomes. The HSRV pol gene is 2,730 nucleotides long, and its deduced protein sequence is readily subdivided into three well-conserved domains, the reverse transcriptase, the RNase H, and the integrase. Although the degree of homology of the HSRV reverse transcriptase domain is highest to that of murine leukemia virus, the HSRV genomic organization is more similar to that of human and simian immunodeficiency viruses. The data justify classifying the spumaretroviruses as a third subfamily of Retroviridae.
Record Date Created: 19880526

6/7/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res

0262606 DBA Accession No.: 2001-02182 PATENT
Treating reverse-transcriptase-mediated disorders, e.g. human immunodeficiency virus (HIV)-1, comprises using nucleotide analogs that control fidelity and execution of reverse-transcriptase - method is useful for treating disease
AUTHOR: Derrien V; Reiss C
CORPORATE SOURCE: Paris Cedex, France.
PATENT ASSIGNEE: CNRS 2000
PATENT NUMBER: WO 200067698 PATENT DATE: 20001116 WPI ACCESSION NO.:
2000-679787 (2066)
PRIORITY APPLIC. NO.: FR 995905 APPLIC. DATE: 19990510
NATIONAL APPLIC. NO.: WO 2000FR1260 APPLIC. DATE: 20000510
LANGUAGE: French
ABSTRACT: A method for preparing a medicament of treating reverse-transcriptase (EC-2.7.7.49) (RT)-mediated disorders is claimed.

It involves using nucleotide analogs (I), accepted as substrate for RT, where (I) includes an optionally protected 3-hydroxy group, on C-3 of 2'-deoxyribose, which can exchange phosphodiester bonds with the forming chain and the obtained nucleotide, and (I) does not terminate the reverse transcription reaction. (I) introduce mis-pairings (especially involving wobble, ANTI-SYN, Hoogsten or reverse Hoogsten or reverse Watson-Crick pairing) into the polynucleotide chain on incorporation by RT. Also claimed is a pharmaceutical composition containing (I) and carrier. (I) is useful for treating retro viral infections in humans, animal or plant, specifically lenti virus, RNA onco virus, spuma virus or hepadna virus infections in HIV virus-1, human t-lymphocyte leukemia virus or hepatitis B virus. (81pp)

? t s8/7/4

8/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10461787 20080982 PMID: 10612669

Construction of infectious feline foamy virus genomes: cat antisera do not cross-neutralize feline foamy virus chimera with serotype-specific Env sequences.

Zemba M; Alke A; Bodem J; Winkler IG; Flower RL; Pfrepper K; Delius H; Flugel RM; Lochelt M

Forschungsschwerpunkt Angewandte Tumorvirologie, Deutsches Krebsforschung szentrum, Heidelberg, 69009, Germany.

Virology (UNITED STATES) Jan 5 2000, 266 (1) p150-6, ISSN 0042-6822 Journal Code: XEA

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Full-length genomes of the feline foamy virus (FFV or FeFV) isolate FUV were constructed. DNA clone pFeFV-7 stably directed the expression of infectious FFV progeny virus indistinguishable from wild-type, uncloned FFV isolate FUV. The env and bel 1 genes of pFeFV-7 were substituted for by corresponding sequences of the FFV serotype 951 since previous studies implicated a defined part of FFV Env protein as responsible for serotype-specific differences in serum neutralization (I. G. Winkler, R. M. Flugel, M. Lochelt, and R. L. P. Flower, 1998. Virology 247: 144-151). Recombinant virus derived from chimeric plasmid pFeFV-7/951 containing the hybrid env gene and the parental clone pFeFV-7 were used for neutralization studies. By means of a rapid titration assay for FFV infectivity, we show that progeny virus derived from plasmid pFeFV-7 was neutralized by FUV- but not by 951-specific antisera, whereas pFeFV-7/951-derived chimeric virus was neutralized by 951-specific antisera only. Both recombinant proviruses will be useful for repeated delivery of foreign genes for therapeutic gene applications into cats. Copyright 2000 Academic Press.

Record Date Created: 20000201

? t s8/7/5 6 8 17-19

8/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10091237 99170716 PMID: 10069948

Specific binding of recombinant foamy virus envelope protein to host cells correlates with susceptibility to infection.

Herchenroder O; Moosmayer D; Bock M; Pietschmann T; Rethwilm A; Bieniasz PD; McClure MO; Weis R; Schneider J

Abteilung Virologie, Institut fur Medizinische Mikrobiologie und Hygiene, University of Freiburg, Freiburg, Germany. herchen@hpi.uni-hamburg.de

Virology (UNITED STATES) Mar 15 1999, 255 (2) p228-36, ISSN 0042-6822 Journal Code: XEA

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The interaction of simian foamy viruses (FVs) with their putative cellular receptor(s) was studied with two types of recombinant envelope protein (Env). Transient expression of full-length Env in BHK-21 cells induced syncytia formation. However, selected stable transfectants fused with naive cells but not with each other. A soluble fusion protein of the Env surface domain with the Fc fragment of a human IgG1 heavy chain (EnvSU-Ig) was produced in the baculovirus expression system, purified to homogeneity, and used for binding and competition analyses. EnvSU-Ig but not unrelated Ig fusion proteins bound to cells specifically. Neutralizing serum blocked binding of EnvSU-Ig and, vice versa, serum-mediated neutralization was abrogated by the chimeric protein. Concomitant reduction of EnvSU-Ig binding and FV susceptibility was seen in Env-expressing target cells. Although EnvSU-Ig did not inhibit FV infection, very likely due to its displacement by multivalent virus-cell interactions, this divalent ligand should help to characterize functionally and to identify the ubiquitous FV receptor. Copyright 1999 Academic Press.

Record Date Created: 19990422

8/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09920369 98440567 PMID: 9765448

Importance of basic residues in the nucleocapsid sequence for retrovirus Gag assembly and complementation rescue.

Bowzard JB; Bennett RP; Krishna NK; Ernst SM; Rein A; Wills JW

Department of Microbiology and Immunology, The Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033, USA.

Journal of virology (UNITED STATES) Nov 1998, 72 (11) p9034-44, ISSN 0022-538X Journal Code: KCV

Contract/Grant No.: CA47482, CA, NCI; CA60395, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The Gag proteins of Rous sarcoma virus (RSV) and human immunodeficiency virus (HIV) contain small interaction (I) domains within their nucleocapsid

(NC) sequences. These overlap the zinc finger motifs and function to provide the proper density to viral particles. There are two zinc fingers and at least two I domains within these Gag proteins. To more thoroughly characterize the important sequence features and properties of I domains, we analyzed Gag proteins that contain one or no zinc finger motifs. Chimeric proteins containing the amino-terminal half of RSV Gag and various portions of the carboxy terminus of murine leukemia virus (MLV) (containing one zinc finger) Gag had only one I domain, whereas similar chimeras with human foamy virus (HFV) (containing no zinc fingers) Gag had at least two. Mutational analysis of the MLV NC sequence and inspection of I domain sequences within the zinc-fingerless C terminus of HFV Gag suggested that clusters of basic residues, but not the zinc finger motif residues themselves, are required for the formation of particles of proper density. In support of this, a simple string of strongly basic residues was found to be able to substitute for the RSV I domains. We also explored the possibility that differences in I domains (e.g., their number) account for differences in the ability of Gag proteins to be rescued into particles when they are unable to bind to membranes. Previously published experiments have shown that such membrane-binding mutants of RSV and HIV (two I domains) can be rescued but that those of MLV (one I domain) cannot. Complementation rescue experiments with RSV-MLV chimeras now map this difference to the NC sequence of MLV. Importantly, the same RSV-MLV chimeras could be rescued by complementation when the block to budding was after, rather than before, transport to the membrane. These results suggest that MLV Gag molecules begin to interact at a much later time after synthesis than those of RSV and HIV.
Record Date Created: 19981105

8/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09322142 97296293 PMID: 9151877
Efficient pseudotyping of murine leukemia virus particles with chimeric human foamy virus envelope proteins.
Lindemann D; Bock M; Schweizer M; Rethwilm A
Institut fur Virologie und Immunobiologie, Wurzburg, Germany. viro066@rzbox.uni-wuerzburg.de
Journal of virology (UNITED STATES) Jun 1997, 71 (6) p4815-20, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Incorporation of human foamy virus (HFV) envelope proteins into murine leukemia virus (MuLV) particles was studied in a transient transfection packaging cell system. We report here that wild-type HFV envelope protein can pseudotype MuLV particles, albeit at low efficiency. Complete or partial removal of the HFV cytoplasmic tail resulted in an abolishment or reduction of HFV-mediated infectivity, implicating a role of the HFV envelope cytoplasmic tail in the pseudotyping of MuLV particles. Mutation of the endoplasmic reticulum retention signal present in the HFV envelope cytoplasmic tail did not result in a higher relative infectivity of pseudotyped retroviral vectors. However, a chimeric envelope protein, containing an unprocessed MuLV envelope cytoplasmic domain fused to a truncated HFV envelope protein, showed an enhanced HFV specific infectivity as a result of an increased incorporation of chimeric envelope proteins into MuLV particles.
Record Date Created: 19970609

8/7/17 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res
(c) 2002 Thomson Derwent & ISI. All rts. reserv.
0268079 DBA Accession No.: 2001-07833 PATENT
Pseudotyped viral particle comprising a functional, modified foamy virus envelope protein, useful as a gene delivery vector - using plasmid pCHFVwt for gene therapy
AUTHOR: Lindemann D; Rethwilm A
CORPORATE SOURCE: Strasbourg, France.
PATENT ASSIGNEE: Transgene 2000
PATENT NUMBER: US 6150138 PATENT DATE: 20001121 WPI ACCESSION NO.:
2001-201505 (2020)
PRIORITY APPLIC. NO.: US 305086 APPLIC. DATE: 19990504
NATIONAL APPLIC. NO.: US 305086 APPLIC. DATE: 19990504
LANGUAGE: English
ABSTRACT: A pseudotyped virus particle (I) containing a functional, modified foamy virus (FV) envelope protein expressed by a vector is claimed. Also claimed are an isolated mammalian cell infected with (I) and a method for treating a disease involving administrating (I). In an example, a eukaryotic expression construct for the envelope gene of the human foamy virus isolate was generated by inserting a 3,076 bp AflII/EcoRI fragment of the virus provirus clone, plasmid pHSRV1 containing the full-length envelope open reading frame into plasmid pCDNA3 vector, resulting in plasmid pCHFVwt that was used to generate mutant and chimeric virus envelope protein. (I) is produced by introducing the recombinant retro virus vector into a cell and culturing the medium. The expressed protein is recovered form the culture medium. The above can be used for a gene delivery vector in gene therapy applications. (11pp)

8/7/18 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res
(c) 2002 Thomson Derwent & ISI. All rts. reserv.
0259614 DBA Accession No.: 2000-14104 PATENT
New vector for the expression of a foamy virus envelope protein, useful for preparing a pseudotyped viral particle, especially for treating a

genetic disorder or a disease induced by any pathogenic gene - plasmid pCHFV-mediated gene transfer and expression in host cell for recombinant vaccine, nucleic acid vaccine and gene therapy
AUTHOR: Rethwilm A; Lindemann D; Winter A J
CORPORATE SOURCE: Strasbourg, France.
PATENT ASSIGNEE: Transgene 2000
PATENT NUMBER: US 6111087 PATENT DATE: 20000829 WPI ACCESSION NO.:
2000-564770 (2052)
PRIORITY APPLIC. NO.: US 42012 APPLIC. DATE: 19980313
NATIONAL APPLIC. NO.: US 42012 APPLIC. DATE: 19980313
LANGUAGE: English
ABSTRACT: A vector for the expression of a fusion protein with a functional, modified foamy virus (FV) envelope protein and all or part of a non-FV envelope protein, is claimed. The fusion is: within the transmembrane (TM) anchor domain of the FV and non-FV envelope proteins; within the cleavage site of the FV and non-FV envelope proteins; or at the junction between the TM anchor domain and the cytoplasmic (CP) domain, or within the CP domains of the FV and non-FV envelope proteins. Also claimed is a complementation cell line (e.g. 293 cell) with the vector. The vector and the cell line are useful for preparing a pseudotyped viral particle. The vector, cell or pseudotyped virus particle is useful for treating a genetic disorder or a disease induced by any pathogenic gene. The above has applications in gene therapy. In an example, A construct designated plasmid pCHFV containing the envelope gene of human-foamy virus (HFV) was used to generate chimeric HFV envelope proteins. Chimeric constructs were made by using polymerase chain reaction on HFV and/or mouse Moloney-leukemia virus env genes as templates and incorporating the desired mutations. (21pp)

8/7/19 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res
(c) 2002 Thomson Derwent & ISI. All rts. reserv.
0229215 DBA Accession No.: 98-10812 PATENT
DNA construct for expressing modified foamy virus envelope protein - for producing FV-pseudotyped retro virus vectors
AUTHOR: Rethwilm A; Lindemann D
CORPORATE SOURCE: Cedex, France.
PATENT ASSIGNEE: Transgene 1998
PATENT NUMBER: EP 864652 PATENT DATE: 980916 WPI ACCESSION NO.: 98-469236
(9841)
PRIORITY APPLIC. NO.: EP 97400573 APPLIC. DATE: 970314
NATIONAL APPLIC. NO.: EP 97400573 APPLIC. DATE: 970314
LANGUAGE: English
ABSTRACT: A DNA construct for the expression of a modified foamy virus (FV) envelope protein is claimed. Also claimed are: a protein expressed by the construct; a pseudotyped virus particle containing a FV envelope protein; a complementation cell line containing the construct; a method for producing the pseudotyped viral particle comprising introducing a recombinant retro virus vector into the complementation cell line, culturing and recovering the pseudotyped viral particle from the culture; and a mammal cell infected with the pseudotyped viral particle. FV-pseudotyped retro virus vectors or mammalian cells infected with them can be used for vaccination or gene therapy e.g. of genetic disorders, cancer or virus-induced disease. The broad host range of FVs, their resistance to inactivation by human serum, and their ability to efficiently infect various cell types, should make mouse leukemia virus (preferred) (MuLV)-based retro virus vectors pseudotyped with the HFV-D2MuLV (HFV envelope protein with the cytoplasmic domain partly deleted and fused to a MuLV domain) chimeric envelope protein a useful tool for efficient gene transfer into various cell types. (18pp)
? t s10/7/2-6 7 9-12
10/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10754405 98440551 PMID: 9765432
High-titer human immunodeficiency virus type 1-based vector systems for gene delivery into nondividing cells.
Mochizuki H; Schwartz JP; Tanaka K; Brady RO; Reiser J
Molecular and Medical Genetics Section, Developmental and Metabolic Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892, USA.
Journal of virology (UNITED STATES) Nov 1998, 72 (11) p8873-83, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Previously we designed novel pseudotyped high-titer replication defective human immunodeficiency virus type 1 (HIV-1) vectors to deliver genes into nondividing cells (J. Reiser, G. Harmison, S. Kluepfel-Stahl, R. O. Brady, S. Karlsson, and M. Schubert, Proc. Natl. Acad. Sci. USA 93:15266-15271, 1996). Since then we have made several improvements with respect to the safety, flexibility, and efficiency of the vector system. A three-plasmid expression system is used to generate pseudotyped HIV-1 particles by transient transfection of human embryonic kidney 293T cells with a defective packaging construct, a plasmid coding for a heterologous envelope (Env) protein, and a vector construct harboring a reporter gene such as neo, ShlacZ (encoding a phleomycin resistance/beta-galactosidase fusion protein), HSA (encoding mouse heat-stable antigen), or EGFP (encoding enhanced green fluorescent protein). The packaging constructs lack functional Vif, Vpr, and Vpu proteins and/or a large portion of the Env coding region as well as the 5' and 3' long terminal repeats, the Nef function, and the presumed packaging signal. Using G418 selection, we

routinely obtained vector particles pseudotyped with the vesicular stomatitis virus G glycoprotein (VSV-G) with titers of up to 8 x 10(7) CFU/microgram of p24, provided that a functional Tat coding region was present in the vector. Vector constructs lacking a functional Tat protein yielded titers of around 4 x 10(6) to 8 x 10(6) CFU/microgram of p24. Packaging constructs with a mutation within the integrase (IN) core domain profoundly affected colony formation and expression of the reporter genes, indicating that a functional IN protein is required for efficient transduction. We explored the abilities of other Env proteins to allow formation of pseudotyped HIV-1 particles. The rabies virus and Mokola virus G proteins yielded high-titer infectious pseudotypes, while the human foamy virus Env protein did not. Using the improved vector system, we successfully transduced contact-inhibited primary human skin fibroblasts and postmitotic rat cerebellar neurons and cardiac myocytes, a process not affected by the lack of the accessory proteins.
Record Date Created: 19981105

10/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10264289 99394673 PMID: 10466797
Properties of human foamy virus relevant to its development as a vector for gene therapy.
Hill CL; Bieniasz PD; McClure MO
Department of GU Medicine and Communicable Diseases, Jefferiss Research Trust Laboratories, Imperial College School of Medicine at St. Mary's, London, UK.
Journal of general virology (ENGLAND) Aug 1999, 80 (Pt 8) p2003-9, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The Spumaviridae (foamy viruses) are increasingly being considered as potential vectors for gene therapy, yet little has been documented of their basic cell biology. This study demonstrates that human foamy virus (HFV) has a broad tropism and that the receptor for HFV is expressed not only on many mammalian, but on avian and reptilian cells. Receptor interference assays using an envelope-expressing cell line and a vesicular stomatitis virus/HFV pseudotype virus demonstrate that the cellular receptor is common to all primate members of the genus. The majority of foamy virus particles assemble and remain sequestered intracellularly. A rapid and quantitative method of assaying foamy virus infectivity by reverse transcriptase activity facilitates the use of classical protocols to increase infectious virus titres in vitro to > or = 10(6) TCID/ml.
Record Date Created: 19990927

10/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10119692 99214398 PMID: 10196355
Packaging cell lines for simian foamy virus type 1 vectors.
Wu M; Mergia A
Department of Pathobiology, College of Veterinary Medicine, University of Florida, Gainesville, Florida 32610, USA.
Journal of virology (UNITED STATES) May 1999, 73 (5) p4498-501, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: AI39126, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Foamy viruses are nonpathogenic retroviruses that offer several unique opportunities for gene transfer in various cell types from different species. We have previously demonstrated the utility of simian foamy virus type 1 (SFV-1) as a vector system by transient expression assay (M. Wu et al., J. Virol. 72:3451-3454, 1998). In this report, we describe the first stable packaging cell lines for foamy virus vectors based on SFV-1. We developed two packaging cell lines in which the helper DNA is placed under the control of either a constitutive cytomegalovirus (CMV) immediate-early gene or inducible tetracycline promoter for expression. Although the constitutive packaging expressing cell line had a higher copy number of packaging DNA, the inducible packaging cell line produced four times more vector particles. This result suggested that the structural gene products in the constitutively expressing packaging cell line were expressed at a level that is not toxic to the cells, and thus vector production was reduced. The SFV-1 vector in the presence of vesicular stomatitis virus envelope protein G (VSV-G) produced an insignificant level of transduction, indicating that foamy viruses could not be pseudotyped with VSV-G to generate high-titer vectors. The availability of stable packaging cell lines represents a step toward the use of an SFV-1 vector delivery system that will allow scaled-up production of vector stocks for gene therapy.
Record Date Created: 19990519

10/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10105327 99173953 PMID: 10074106
Foamy virus capsids require the cognate envelope protein for particle export.
Pietschmann T; Heinkelein M; Heldmann M; Zentgraf H; Rethwilm A; Lindemann D
Institut fur Virologie und Immunbiologie, Germany.
Journal of virology (UNITED STATES) Apr 1999, 73 (4) p2613-21, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Unlike other subclasses of the Retroviridae the Spumavirinae, its

prototype member being the so-called human foamy virus (HFV), require the expression of the envelope (Env) glycoprotein for viral particle egress. Both the murine leukemia virus (MuLV) Env and the vesicular stomatitis virus G protein, which efficiently pseudotype other retrovirus capsids, were not able to support export of HFV particles. Analysis of deletion and point mutants of the HFV Env protein revealed that the HFV Env cytoplasmic domain (CyD) is dispensable for HFV particle envelopment, release, and infectivity, whereas deletion of the membrane-spanning-domain (MSD) led to an accumulation of naked capsids in the cytoplasm. Neither alternative membrane association of HFV Env deletion mutants lacking the MSD and CyD via phosphoglycolipid anchor nor domain swapping mutants, with the MSD or CyD of MuLV Env and VSV-G exchanged against the corresponding HFV domains, could restore particle envelopment and the release defect of pseudotypes. However, replacement of the HFV MSD with that of MuLV led to budding of HFV capsids at the intracellular membranes. These virions were of apparently wild-type morphology but were not naturally released into the supernatant and they were noninfectious.
Record Date Created: 19990506

10/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
09929822 98445459 PMID: 9770433
Cells expressing the human foamy virus (HFV) accessory Bet protein are resistant to productive HFV superinfection.
Bock M; Heinkelein M; Lindemann D; Rethwilm A
Institut fur Virologie und Immunbiologie, Universitat Wurzburg, Versbacher Str.7, Wurzburg, 97078, Germany.
Virology (UNITED STATES) Oct 10 1998, 250 (1) p194-204, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Bet is a foamy virus (FV) accessory protein not required for virus replication. The function of Bet is not understood. We report on the generation of cell lines stably expressing the HFV Bet protein. In Bet+ cells, HFV replication was reduced by approximately 3-4 orders of magnitude compared with control cells. The HFV Bet-expressing cells only partially resisted infection by the distantly related feline FV (FFV). Pseudotyping experiments, using murine retroviral vectors with an HFV envelope, revealed that the resistance was not due to downregulation of the unknown HFV receptor. In transfection experiments, using proviral reporter gene constructs and infectious proviruses, no significant differences were detected between Bet+ and control cells. In infection experiments, HFV vectors expressing an indicator gene under control of the HFV promoters showed no activity in Bet+ cells. The results are best compatible with the hypothesis that the main block to productive superinfection of Bet+ cells occurs at an early stage of replication between virus entry and provirus establishment. We suggest that inhibition of provirus integration by Bet protein may serve a distinct function in the unique foamy virus replication cycle. Copyright 1998 Academic Press.
Record Date Created: 19981105

10/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
03971904 82169396 PMID: 6279771
Simian foamy virus pseudotypes of vesicular stomatitis virus: production and use in sero-epidemiological investigations.
Schnitzer TJ
Journal of general virology (ENGLAND) Mar 1982, 59 (Pt 1) p203-6, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Simian foamy virus (SFV) pseudotypes of vesicular stomatitis virus have been successfully produced and their host range characterized. The availability of these pseudotypes has permitted the development of a rapid, quantitative assay to measure neutralizing antibody titres to SFV that has proved useful in a sero-epidemiological study.
Record Date Created: 19820614

10/7/9 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res
(c) 2002 Thomson Derwent & ISI. All rts. reserv.
0240905 DBA Accession No.: 99-10479
Properties of human foamy virus relevant to its development as a vector for gene therapy - retro virus vector
AUTHOR: Hill C L; Bieniasz P D; McClure M O
CORPORATE AFFILIATE: Univ.London St.Mary's-Hosp.London
CORPORATE SOURCE: Department of GU Medicine and Communicable Diseases, Jefferiss Research Trust Laboratories, Imperial College School of Medicine at St. Mary's, Praed Street, London W2 1NY, UK. email:m.mcclure@ic.ac.uk
JOURNAL: J.Gen.Virol. (80, Pt.8, 2003-09) 1999
ISSN: 0022-1317 CODEN: JGVIAY
LANGUAGE: English
ABSTRACT: The Spumaviridae, foamy viruses, are increasingly being used as potential vectors for gene therapy, despite the lack of documentation on their basic cell biology. The human foamy virus was shown to have a broad tropism and the receptor for human foamy virus is expressed not only on many mammalian, but on bird and reptilian cells. Receptor interference assays using an envelope-expressing cell line and a vesicular-stomatitis virus/human foamy virus pseudotype virus showed that the cellular receptor was common to all primate members of the genus. Most foamy virus particles assembled and remained sequestered

intracellularly. A rapid and quantitative method of assaying foamy virus infectivity by reverse-transcriptase activity facilitated the use of classical protocols to increase infectious virus titers in vitro to over 1 million TCID/ml. Human foamy viruses should be useful for gene transfer to a wide variety of host cells. Foamy viruses can be produced in reasonable amounts and can be concentrated without loss of infectivity. (34 ref)

10/7/10 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res

0236980 DBA Accession No.: 99-07081
Packaging cell lines for simian foamy virus type 1 vectors - 293-3 cell culture used as simian-foamy virus packaging cell culture for production of nonpathogenic virus vector for gene therapy
AUTHOR: Wu M; +Mergia A
CORPORATE AFFILIATE: Univ.Florida
CORPORATE SOURCE: Department of Pathobiology, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610, USA. email:mergiaa@mail.vetmed.ufl.edu
JOURNAL: J.Virol. (73, 5, 4498-501) 1999
ISSN: 0022-538X CODEN: JOVIAM
LANGUAGE: English
ABSTRACT: Foamy viruses are retro viruses with no pathogenic activity that offer a range of unique opportunities for gene transfer. Simian-foamy virus type-1 (SFV-1) has been shown to be useful as a vector system by transient expression assay. Stable packaging cells used to produce foamy virus vectors based on SFV-1 were then developed. This involved developing packaging cell cultures in which helper DNA was controlled by a constitutive cytomegalo virus immediate-early gene promoter, or an inducible tetracycline promoter. The constitutive packaging cell line had the larger packaging DNA number but the inducible cell line produced four times as many vector particles. This suggested the structural gene products in the constitutive cell line were expressed at non toxic levels, reducing vector mediated production. The SFV-1 vector produced insignificant amounts of transduction in the presence of vesicular-stomatitis virus envelope protein-G, suggesting foamy virus can not be pseudotyped to that protein to produce high-titer vectors. A stable packaging cell line allows scaled up vector production for SFV-1 mediated gene therapy. (34 ref)

10/7/11 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res

0232771 DBA Accession No.: 99-02872 PATENT
Transducing mammalian cells ex vivo - retro virus vector-mediated human B-domain-deleted Factor-VIII gene transfer, used for blood disorder gene therapy
AUTHOR: Vanden Driessche T; Chuah M K L
CORPORATE SOURCE: Louvain, Belgium.
PATENT ASSIGNEE: Louvain-Res.Develop. 1998
PATENT NUMBER: WO 9853063 PATENT DATE: 981126 WPI ACCESSION NO.: 99-070148 (9906)
PRIORITY APPLIC. NO.: EP 98200382 APPLIC. DATE: 980209
NATIONAL APPLIC. NO.: WO 98EP3013 APPLIC. DATE: 980518
LANGUAGE: English
ABSTRACT: A method for the ex vivo transduction of mammalian cells, preferably bone marrow (BM) stromal cells, also other specified BM cells or cells belonging to the lymphohemato-poietic lineage, fibroblast, endothelial cells, chondroblasts, chondrocytes, myoblasts, myocytes, osteoblasts, epithelia cells, keratinocytes, mesenthelial cells or hepatocytes, is new, and involves transduction using an intron based retro virus vector (e.g. mouse Maloney leukemia virus, gibbon ape leukemia virus, Rous-sarcoma virus, myeloproliferative sarcoma virus, lenti virus, human foamy virus, HIV virus, SIV virus or cattle leukemia virus) containing a B-domain-deleted human Factor-VIII cDNA or other specified factors. The transduction involves pseudotyping the vector with a gibbon ape leukemia virus envelope and cell phosphate starvation. Also claimed are the genetically engineered cells which can be used in coagulation blood disorder gene therapy particularly hemophilia-A and to treat bone marrow osteoporosis, osteogenesis imperfecta, chondrodyplasia, arthritis and cancer. (34pp)

10/7/12 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res

0229311 DBA Accession No.: 98-10908 PATENT
Construct for the expression of a modified foamy virus envelope protein - retro virus vector expression in complementation cell culture and mammal cell infection for pseudotyped virus particle production; application in disease therapy
AUTHOR: Rethwilm A; Lindemann D; Winter A J
CORPORATE SOURCE: Strasbourg, France.
PATENT ASSIGNEE: Transgene 1998
PATENT NUMBER: WO 9840507 PATENT DATE: 980917 WPI ACCESSION NO.: 98-506737 (9843)
PRIORITY APPLIC. NO.: CA 199989 APPLIC. DATE: 970313
NATIONAL APPLIC. NO.: WO 98IB343 APPLIC. DATE: 980313
LANGUAGE: English
ABSTRACT: A construct (A) for the expression of a protein, characterized in that the protein contains at least a modified (mutation or truncation at residue 975 or 981) human foamy virus (HFV) envelope protein, is new. Also claimed are: a protein expressed by (A); a pseudotyped viral particle (VP) containing a HFV envelope protein, or the protein above;

a complementation cell line containing (A); and a mammalian cell infected with the pseudotyped VP. The protein is a fusion protein containing all or part of a non-HFV envelope protein. The non-HFV envelope protein is derived from Moloney leukemia virus (MLV), mouse MLV, FB29, HIV virus or SIV virus. The protein preferably contains the extracellular domain and the 5' part of the transmembrane anchor domain of the HFV envelope protein and the 3' part of the transmembrane anchor domain and the cytoplasmic domain of the non-HFV envelope protein, particularly the SIV virus envelope protein. The pseudotyped VP can be prepared by: introducing a recombinant retro virus vector into the complementation cell; culturing the cell; and recovering the particle. The above may be used for disease therapy. (49pp)

? t s12/7/7

12/7/7 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res
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0240950 DBA Accession No.: 99-10524 PATENT
Pseudo-type retro virus vectors with modified surface capsid proteins - recombinant virus vector construction with modified surface capsid protein for, e.g. HIV virus-1 and cystic fibrosis diagnosis, gene therapy and use as a recombinant vaccine
AUTHOR: Cichutek K; Merget-Millitzer H
CORPORATE SOURCE: Langen, Germany.
PATENT ASSIGNEE: Inst.Paul-Ehrlich 9999
PATENT NUMBER: WO 9928488 PATENT DATE: 99990610 WPI ACCESSION NO.:
99-358132 (9930)
PRIORITY APPLIC. NO.: -1 9752855 APPLIC. DATE: 97-91128
NATIONAL APPLIC. NO.: WO 98 a3542 APPLIC. DATE: 98 a1127
LANGUAGE: German
ABSTRACT: Pseudo-type retro virus vectors with modified surface capsid proteins are new. The vector essentially consists of a virus core chosen from the group of mouse leukemia virus (MLV), HIV virus, sheep immunodeficiency virus (SIV), menti virus or foamy virus and a virus capsid protein from spleen-necrosis virus. Also claimed is a retro virus packaging cell for the new retro virus vector and also transformed with one or more psi-negative expression constructs, the gag and pol gene products of MLV, HIV, SIV or foamy virus, or also with a psi-negative SNV-env expression construct and/or psi-negative SNV-ENV foreign protein-SNV-HIV-ENV or SNV-SIV-ENV expression construct. The pseudo-type retro virus vectors with modified surface capsid proteins may be useful for cell-specific transduction of a selected mammal cell type (cell targeting). The methods may be useful for the production of the vectors and for use in gene transfer to selected cell types. The vectors may be used for diagnosis vaccination and gene therapy. The vectors may be used to specifically treat cystic fibrosis, HIV virus-1 infection, ADA-deficiency and chronic granulomatosis. (41pp)

? ds

Set	Items	Description
S1	43936	HEPATITIS(W)B OR HBV OR HEPADNAVIR?
S2	1467	FOAMY
S3	11	S1 AND S2
S4	433	SPUMA?
S5	12	S1 AND S4
S6	2	S5 NOT S3
S7	34707	CHIMER? OR CHIMAER? OR PSEUDOVIR?
S8	22	S7 AND (S2 OR S4)
S9	1035	PSEUDOTYP?
S10	12	S9 AND (S2 OR S4) NOT S8
S11	10	RD (unique items)
S12	7	PSEUDO AND (S2 OR S4)

? s pseudo? and retrovir? and s1
>>>File 155 processing for PSEUDO? stopped at PSEUDOFIBRINOLYSIS
44865 PSEUDO?
29370 RETROVIR?
43936 S1
S13 4 PSEUDO? AND RETROVIR? AND S1
? t s13/6/1-4

13/6/1 (Item 1 from file: 357)
0276261 DBA Accession No.: 2001-15927
Murine retro viral pseudotyped virus containing hepatitis B virus large and small surface antigens confers specific tropism for primary human hepatocytes: a potential liver-specific targeting system - plasmid pCMV-L, and plasmid pCMV-S expression in 293 cell useful in gene therapy 2001

13/6/2 (Item 2 from file: 357)
0275720 DBA Accession No.: 2001-15927
Murine retro viral pseudotyped virus containing hepatitis B virus large and small surface antigens confers specific tropism for primary human hepatocytes: a potential liver-specific targeting system - plasmid pCMV-L, and plasmid pCMV-S expression in 293 cell useful in gene therapy 2001

13/6/3 (Item 3 from file: 357)
0196248 DBA Accession No.: 96-07019
Production of transgenic dwarf surfclams, Mulinia lateralis, with pantropic retroviral vectors - clam transgenic animal production by electroporation with a retro virus vector 1996

13/6/4 (Item 4 from file: 357)
0177113 DBA Accession No.: 95-03934
Efficient in vivo transduction of the neonatal mouse liver with pseudotyped retroviral vectors - hepatitis B virus surface antigen gene expression

in mouse liver using retro virus vector, for application in liver disease gene therapy 1995
? s pseudotyp? or pseudovir?
1035 PSEUDOTYP?
147 PSEUDOVIR?
S14 1178 PSEUDOTYP? OR PSEUDOVIR?
? ds
Set Items Description
S1 43936 HEPATITIS(W)B OR HBV OR HEPADNAVIR?
S2 1467 FOAMY
S3 11 S1 AND S2
S4 433 SPUMA?
S5 12 S1 AND S4
S6 2 S5 NOT S3
S7 34707 CHIMER? OR CHIMAER? OR PSEUDOVIR?
S8 22 S7 AND (S2 OR S4)
S9 1035 PSEUDOTYP?
S10 12 S9 AND (S2 OR S4) NOT S8
S11 10 RD (unique items)
S12 7 PSEUDO AND (S2 OR S4)
S13 4 PSEUDO? AND RETROVIR? AND S1
S14 1178 PSEUDOTYP? OR PSEUDOVIR?
? s 14 and retrovir? and s1
480863 14
29370 RETROVIR?
43936 S1
S15 12 14 AND RETROVIR? AND S1
<------User Break------>

Connecting via Winsock to Dialog

Logging in to Dialog
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
****
ENTER PASSWORD:
****
Welcome to DIALOG

Dialog level 02.03.27D

>>> Cost Estimate prior to Disconnect, information only
>>> 30apr02 10:34:22 User208669 Session D2011.2
>>> $8.43 2.634 DialUnits File155
>>> $0.00 40 Type(s) in Format 6
>>> $4.62 22 Type(s) in Format 7
>>> $4.62 62 Types
>>> $13.05 Estimated cost File155
>>> $8.64 0.506 DialUnits File357
>>> $0.00 16 Type(s) in Format 6
>>> $24.30 9 Type(s) in Format 7
>>> $24.30 25 Types
>>> $32.94 Estimated cost File357
>>> OneSearch, 2 files, 3.140 DialUnits FileOS
>>> $5.20 TELNET
>>> $51.19 Estimated cost this search
>>> $51.48 Estimated total session cost 3.221 DialUnits
>>>
Reconnected in file OS 30apr02 10:34:37
* *

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-2002/Apr W3
*File 155: This file will be reloaded. Accession numbers will change.
File 357:Derwent Biotech Res 1982-2002/Feb w3
(c) 2002 Thomson Derwent & ISI
*File 357: Price changes as of 1/1/02. Please see HELP RATES 357.
Derwent announces file enhancements. Please see HELP NEWS 357.

Set Items Description
--- ----- -----------
Cost is in DialUnits
? t s16/7/2 3
16/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10934409 20514551 PMID: 11058957
Construction of the recombinant retrovirus vector of HBV-S gene and it's expression in eukaryotic cells.
Zhou Z; Zhang D; Ren H
Institute for Viral Hepatitis, Chongqing University of Medical Sciences, Chongqing 400010, China.
Zhonghua gan zang bing za zhi (CHINA) Oct 2000, 8 (5) p296-8, ISSN 1007-3418 Journal Code: DAU
Languages: CHINESE
Document type: Journal Article
Record type: Completed
OBJECTIVE: To investigate the effectiveness of recombinant retrovirus vector in gene therapy. METHODS: The retroviral vector PLXSN-S was constructed and transferred into PA317 by means of electroporation, then HepG(2), P815, and EL4 cells were infected with the pseudovirus produced from PA317, which highly expressed HBsAg. HBsAg expression was tested by RT-PCR and ELISA. RESULTS: HBsAg was expressed variously in the eukaryotic

cells mentioned above. HBsAg (A value) of the cell supernatants (48 h) were 0.92, 0.09, 0.47, respectively. CONCLUSION: The vector used in this study is an effective one to carry genes of interest to target cells and it may be useful in the test for gene therapy.
Record Date Created: 20010125

16/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
10756191 99045631 PMID: 9826647
Transgenic cattle produced by reverse-transcribed gene transfer in oocytes.
Chan AW; Homan EJ; Ballou LU; Burns JC; Bremel RD
Endocrinology-Reproductive Physiology Program, University of Wisconsin, 1675 Observatory Drive, Madison, WI 53706, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov 24 1998, 95 (24) p14028-33, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A critical requirement for integration of retroviruses, other than HIV and possibly related lentiviruses, is the breakdown of the nuclear envelope during mitosis. Nuclear envelope breakdown occurs during mitotic M-phase, the envelope reforming immediately after cell division, thereby permitting the translocation of the retroviral preintegration complex into the nucleus and enabling integration to proceed. In the oocyte, during metaphase II (MII) of the second meiosis, the nuclear envelope is also absent and the oocyte remains in MII arrest for a much longer period of time compared with M-phase in a somatic cell. Pseudotyped replication-defective retroviral vector was injected into the perivitelline space of bovine oocytes during MII. We show that reverse-transcribed gene transfer can take place in an oocyte in MII arrest of meiosis, leading to production of offspring, the majority of which are transgenic. We discuss the implications of this mechanism both as a means of production of transgenic livestock and as a model for naturally occurring recursive transgenesis.
Record Date Created: 19981228
? log hold
30apr02 10:36:20 User208669 Session D2011.3
$0.86 0.270 DialUnits File155
$0.00 6 Type(s) in Format 6
$0.42 2 Type(s) in Format 7
$0.42 8 Types
$1.28 Estimated cost File155
$1.40 0.082 DialUnits File357
$0.00 4 Type(s) in Format 6
$0.00 4 Types
$1.40 Estimated cost File357
OneSearch, 2 files, 0.351 DialUnits FileOS
$0.43 TELNET
$3.11 Estimated cost this search
$3.11 Estimated total session cost 0.351 DialUnits
Logoff: level 02.03.27 D 10:36:20